

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1 (Previously Amended) An oligonucleotide comprising a plurality of nucleotides, wherein:

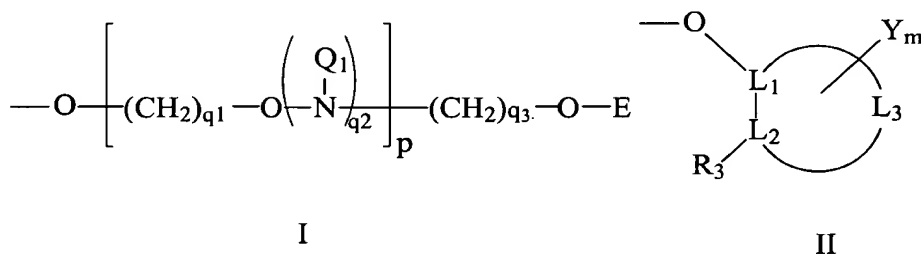
a first portion of said plurality of nucleotides have B-form conformational geometry and are joined together in a continuous sequence, at least two of said nucleotides of said first portion being ribonucleotides; and

a further portion of said plurality of nucleotides are ribonucleotide that have A-form conformation geometry and are joined together in at least one continuous sequence.

2 (Original). The oligonucleotide of claim 1 wherein each nucleotide of said first portion, independently, is a 2'-SCH₃ ribonucleotide, a 2'-NH₂ ribonucleotide, a 2'-NH(C₁-C₂ alkyl) ribonucleotide, a 2'-N(C₁-C₂ alkyl)₂ ribonucleotide, a 2'-CF₃ ribonucleotide, a 2'=CH₂ ribonucleotide, a 2'=CHF ribonucleotide, a 2'=CF₂ ribonucleotide, a 2'-CH₃ ribonucleotide, a 2'-C₂H₅ ribonucleotide, a 2'-CH=CH₂ ribonucleotide or a 2'-C≡CH ribonucleotide.

3 (Original). The oligonucleotide of claim 1 wherein each of said nucleotides of said first portion are joined together in said continuous sequence by phosphate, phosphorothioate, phosphorodithioate or boranophosphate linkages.

4 (Previously Amended). The oligonucleotide of claim 1 wherein each nucleotide of said further portion, independently, is a 2'-fluoro nucleotide or a nucleotide having a 2'-substituent having the formula I or II:



wherein

E is C₁-C₁₀ alkyl, N(Q₁)(Q₂) or N=C(Q₁)(Q₂);

each Q₁ and Q₂ is, independently, H, C₁-C₁₀ alkyl, dialkylaminoalkyl, a nitrogen protecting group, a tethered or untethered conjugate group, a linker to a solid support, or Q₁ and Q₂, together, are joined in a nitrogen protecting group or a ring structure optionally containing at least one additional heteroatom selected from N and O;

R₃ is OX, SX, or N(X)₂;

each X is, independently, H, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C(=NH)N(H)Z, C(=O)N(H)Z or OC(=O)N(H)Z;

Z is H or C₁-C₈ alkyl;

L₁, L₂ and L₃ form a ring system having from about 4 to about 7 carbon atoms or having from about 3 to about 6 carbon atoms and 1 or 2 heteroatoms selected from oxygen, nitrogen and sulfur

and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic;

Y is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms, N(Q₁)(Q₂), O(Q₁), halo, S(Q₁), or CN;

each q₁ is, independently, from 2 to 10;

each q₂ is, independently, 0 or 1;

m is 0, 1 or 2;

p is from 1 to 10; and

q₃ is from 1 to 10 with the proviso that when p is 0, q₃ is greater than 1.

5 (Original). The oligonucleotide of claim 1 wherein each of said nucleotides of said further portion, independently, is a 2'-F ribonucleotide, a 2'-O-(C₁-C₆ alkyl) ribonucleotide, or a 2'-O-(C₁-C₆ substituted alkyl) ribonucleotide wherein the substitution is C₁-C₆ ether, C₁-C₆ thioether, amino, amino(C₁-C₆ alkyl) or amino(C₁-C₆ alkyl)₂.

6 (Original). The oligonucleotide of claim 1 wherein all of said nucleotides of said further portion are joined together in a continuous sequence by 3'-5' phosphodiester, 2'-5' phosphodiester, phosphorothioate, Sp phosphorothioate, Rp phosphorothioate, phosphorodithioate, 3'-deoxy-3'-

amino phosphoroamidate, 3'-methylenephosphonate, methylene(methylimino), dimethylhydrazino, amide 3, amide 4 or boranophosphate linkages.

7 (Original). The oligonucleotide of claim 1 wherein at least two of said nucleotides of said further portion are joined together in a continuous sequence that is positioned 3' to said continuous sequence of said first portion of said plurality of nucleotides.

8 (Original). The oligonucleotide of claim 1 wherein at least two of said nucleotides of said further portion are joined together in a continuous sequence that is positioned 5' to said continuous sequence of said first portion.

9 (Original). The oligonucleotide of claim 1 wherein at least two of said nucleotides of said further portion are joined together in a continuous sequence that is positioned 3' to said continuous sequence of said first portion and at least two of said further portion are joined together in a continuous sequence that is positioned 5' to said continuous sequence of said first portion.

10 (Original). The oligonucleotide of claim 1 wherein each nucleotide of said first portion, independently, is a 2'-SCH₃ ribonucleotide, a 2'-NH₂ ribonucleotide, a 2'-NH(C₁-C₂ alkyl) ribonucleotide, a 2'-N(C₁-C₂ alkyl)₂ ribonucleotide, a 2'=CH₂ ribonucleotide, a 2'-CH₃ ribonucleotide,

a 2'-C₂H₅ ribonucleotide, a 2'-CH=CH₂ ribonucleotide or a 2'-C≡CH ribonucleotide.

11 (Original). The oligonucleotide of claim 1 wherein each nucleotide of said first portion, independently, is a 2'-SCH₃ ribonucleotide, a 2'-NH₂ ribonucleotide a 2'-NH(C₁-C₂ alkyl) ribonucleotide, a 2'-N(C₁-C₂ alkyl)₂ ribonucleotide or a 2'-CH₃ ribonucleotide.

12 (Original). The oligonucleotide of claim 1 wherein each nucleotide of said first portion, independently, is a 2'-SCH₃ ribonucleotide, a 2'-NH₂ ribonucleotide or a 2'-CH₃ ribonucleotide.

13 (Original). The oligonucleotide of claim 1 wherein each nucleotide of said first portion is a 2'-SCH₃ ribonucleotide.

Claims 14-17 (Canceled).

18 (Original). The oligonucleotide of claim 1 wherein each nucleotide of said first portion, independently, is a 2'-SCH₃ ribonucleotide, a 2'-NH₂ ribonucleotide a 2'-NH(C₁-C₂ alkyl) ribonucleotide, a 2'-N(C₁-C₂ alkyl)₂ ribonucleotide, a 2'-CH₃ ribonucleotide, a 2'-CH=CH₂ ribonucleotide or a 2'-C≡CH ribonucleotide; and

each nucleotide of said further portion, independently, is a 2'-F ribonucleotide, a 2'-O-(C₁-C₆

alkyl) ribonucleotide, or a 2'-O-(C₁-C₆ substituted alkyl) ribonucleotide wherein the substitution is C₁-C₆ ether, C₁-C₆ thioether, amino, amino(C₁-C₆ alkyl) or amino(C₁-C₆ alkyl)₂.

Claims 19-20 (Canceled).

21 (Original). The oligonucleotide of claim 1 wherein said further portion comprises at least two nucleotides joined together in a continuous sequence that is positioned at the 3' terminus end of said oligonucleotide.

22 (Original). The oligonucleotide of claim 1 wherein said further portion comprises at least two nucleotides joined together in a continuous sequence that is positioned at the 5' terminus of said oligonucleotide.

23 (Original). The oligonucleotide of claim 1 wherein said further portion comprises at least two nucleotides joined together in a continuous sequence that is positions at the 3' terminus of said oligonucleotide; and

at least two nucleotides joined together in a continuous sequence that is positions at the 5' terminus of said oligonucleotide.

24 (Original). The oligonucleotide of claim 21 wherein said at least two nucleotides joined together comprise nucleotides joined together by a 2'-5' phosphodiester linkage, a 3'-methylenephosphonate linkage, a Sp phosphorothioate linkage, a methylene(methylimino) linkage, a dimethyhydrazino linkage, a 3'-deoxy-3'-amino phosphoroamidate linkage, an amide 3 linkage or an amide 4 linkage.

25 (Original). The oligonucleotide of claim 24 wherein said two nucleotides are joined together by a 2'-5' phosphodiester linkage, a 3'-methylenephosphonate linkage, a Sp phosphorothioate linkage or a methylene(methylimino) linkage.

26 (Original). The oligonucleotide of claim 22 wherein said at least two nucleotides joined together comprise nucleotides joined together by a 2'-5' phosphodiester linkage, a 3'-methylenephosphonate linkage, a Sp phosphorothioate linkage, a methylene(methylimino) linkage, a dimethyhydrazino linkage, a 3'-deoxy-3'-amino phosphoroamidate linkage, an amide 3 linkage or an amide 4 linkage.

27 (Original). The oligonucleotide of claim 26 wherein said two nucleotides are joined together by a 2'-5' phosphodiester linkage, a 3'-methylenephosphonate linkage, a Sp phosphorothioate linkage or a methylene(methylimino) linkage.

28 (Original). The oligonucleotide of claim 23 wherein said at least two nucleotides joined together and positioned at said 3' terminus comprise nucleotides joined together by a 2'-5' phosphodiester linkage, a 3'-methylenephosphonate linkage, a Sp phosphorothioate linkage, a methylene(methylimino) linkage, a dimethyhydrazino linkage, a 3'-deoxy-3'-amino phosphoroamidate linkage, an amide 3 linkage or an amide 4 linkage; and

wherein said at least two nucleotides joined together and positioned at said 5' terminus comprise nucleotides joined together by a 2'-5' phosphodiester linkage, a 3'-methylenephosphonate linkage, a Sp phosphorothioate linkage, a methylene(methylimino) linkage, a dimethyhydrazino linkage, a 3'-deoxy-3'-amino phosphoroamidate linkage, an amide 3 linkage or an amide 4 linkage.

29 (Original). The oligonucleotide of claim 28 wherein said two nucleotides joined together at said 3' terminus and said two nucleotides joined together at said 5' terminus are, independently, joined together by 2'-5' phosphodiester linkages, 3'-methylenephosphonate linkages, Sp phosphorothioate linkages or methylene(methylimino) linkages.

30 (Original). The oligonucleotide of claim 21 wherein at least one of said two nucleotides joined together is a 2'-alkylamino substituted nucleotide.

31 (Original). The oligonucleotide of claim 22 wherein at least one of said two nucleotides

joined together is a 2'-alkylamino substituted nucleotide.

32 (Original). The oligonucleotide of claim 23 wherein at least one of said two nucleotides joined together at said 3' terminus is a 2'-alkylamino substituted nucleotide, and

wherein at least one of said two nucleotides joined together at said 5' terminus is a 2'-alkylamino substituted nucleotide.

Claims 33-36 (Canceled).